UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,736	10/18/2004	Xavier Billot	MC058YP	2550

210 7590 02/19/2009

MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
02/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,736	BILLOT ET AL.	
	Examiner	Art Unit	
	Sean Basquill	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-19,21,22,27 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-19,21,22,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Previous Rejections

1. Applicants' arguments, filed 26 September and 26 November 2008, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Amendments

2. Claims 1-16, 20, and 23-26 have been cancelled. Amendments to Claims 21 and 22 and new Claims 27 and 28 have been entered. Claims 17-19, 21, 22, 27, and 28 are presented for examination.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 17-19 stand rejected under 35 U.S.C. 103(a) as being obvious over International Application Publication WO01/46140 (hereinafter "Cameron") (of record), in view of International Application Publication WO02/24647 (hereinafter "Maruyama") (of record).

As a threshold matter, applicants are reminded that the instant claims are directed to compounds and compositions, rather than a method of using said compositions, for example, treating any particular disease. Claim language such as "for treating ocular hypertension" has been interpreted as a recitation of an intended use, and is therefore of no significance to the construction of the instant claims. MPEP § 2111.02(II).

Applicant's arguments have been considered and are deemed unpersuasive. Insofar as the examiner has been able to ascertain, applicant's arguments that the compounds of instant Claims 17-19 are neither taught nor suggested by the combination of Cameron and Maruyama amount to the conclusory statement that the instant compounds are neither taught nor suggested.

To reiterate the explanation put forth in the previous action, Cameron discloses a series of E_2 prostaglandins for the prevention of bone loss, particularly agonists of the EP_4 subtype receptor nearly identical to the compound claimed in the instant application (pg. 4, L.10-11), ***except*** that the Cameron PGE_2 lacks the 4,4 -difluoro substitution of the instantly claimed compound. Maruyama discloses agonists of the EP_4 subtype receptor also nearly identical to the instantly claimed compound also useful in the prevention of bone loss (abstract), where the difference constitutes a carboxylic acid terminus to the alpha chain in place of the instantly claimed 1*H*-tetrazol-5-yl group. (Pg. 14). The differences between the claimed compound and that disclosed in Cameron and Maruyama represent straightforward cases of bioisosterism (Camille Wermuth, *Molecular Variations Based on Isosteric Replacements*, THE PRACTICE OF

MEDICINAL CHEMISTRY 204 (1996) (of record)), especially when considered in light of the comparable uses (replacement of bone loss) both compounds are disclosed as capable of. This concomitance of use indicates a comparable physiological effect the comparable structures share, and in light of the evidence provided that either acts as a potent EP_4 subtype receptor agonist, would have been obvious to one of skill in the art at the time of the invention that a combination of the disclosed structures would reasonably result in a compound of potent EP_4 subtype receptor agonism as well.

Applicants have failed to rebut the examiners' assertion that one having ordinary skill in the relevant art, aware of the teachings of both Cameron and Maruyama, would have been motivated to substitute the 4 position of the compound of Cameron with the difluro- moiety described by Maruyama, resulting in the EP4 receptor agonist of the instant claims.

4. Claims 21, 22, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cameron and Maruyama as applied to Claims 17 above, and further in view of International Application Publication WO00/38667 (hereinafter "Klimko") (of record).

While Cameron as modified by Maruyama describe EP4 receptor agonist compounds as provided above, they do not indicate that compositions comprising EP4 receptor agonists such as the instant claimed compound in combination with additional compounds such as the beta-blocker timolol may be used for the treatment of diseases such as ocular hypertension or glaucoma.

Klimko describes the use of EP4 receptor agonists in combination with beta-blockers such as timolol in the reduction of intraocular pressure and the treatment of glaucoma. (Pg. 4).

Klimko additionally indicates that compositions containing these compounds may be formed by the inclusion of the pertinent compounds in pharmaceutically acceptable vehicles yielding a solution for topical ophthalmic administration. (Pg. 16).

Because Cameron and Maruyama disclose bioisosteres of the instant claimed EP_4 subtype receptor agonist, and Klimko teaches that EP4 receptor agonists are effective in treating Glaucoma either alone or in combination with beta-blockers, it would have been prima facie obvious to use the EP4 receptor agonists disclosed in Cameron as modified by Maruyama in a composition capable of treatment of glaucoma alone or in combination with beta blockers such as timolol as described by Klimko. One having ordinary skill in the art would have been motivated to do so because the skilled artisan would recognize that the EP4 receptor agonist of Cameron as modified by Maruyama would provide the same utility as the EP4 receptor agonists described by Klimko as useful for the treatment of glaucoma The compounds share an art-recognized equivalence as EP4 receptor agonists and would be expected to perform similarly by the skilled artisan.

Conclusion

No Claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean Basquill whose telephone number is (571) 270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sean Basquill

Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612